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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/750,879

01/05/2004

Matthias Wicsner

MERCK-2481-P1

3230

23599

7590

07/06/2006

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EXAMINER

SHIAO, REI TSANG

ART UNIT

PAPER NUMBER

1626

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/750,879

Applicant(s)

WIESNER ET AL.

Examiner

Robert Shiao

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 6,10-13 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-9 and 14-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 10/203,406.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This application claims benefit of the foreign application:
GERMANY 10006139.7 with a filing date 02/11/2000.
2. The request to correct the inventorship of this nonprovisional application under 37 CFR 1.48(a) is deficient because: the citizenship (i.e., Briten) of the inventor Simmon Goodman has not been identified.
3. Claims 1-22 are pending in the application.

Responses to Election/Restriction

4. Applicant's election with traverse of Group III claims 1-5, 7-9, and 14-21, in part, in the reply filed on May 08, 2006, is acknowledged. An elected species, i.e., 3-(benzo-[1,2,5] thiadiazol-5-yl)-3-{6-[2-(6-methylamino-pyridin-2-yl)-ethyloxy]-indol-3-yl}-propionic acid, is also acknowledged. The traversal is on the grounds that the Groups I-VIII are related to each other and so the burden on the Examiner to examine the full scope of the claims is far less than the burden on the application to file, and MPEP 803 is cited. This is not found persuasive and reasons are given, *infra*.

Claims 1-22 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-5, 7-9, and 14-21, in part, drawn to a compound/compositions of formula (I or Ij), wherein the variable Het represents benzothiadiazole, 1,3-dioxane,

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indol-2-yl, pyrrol-2-yl, pyridin-4-yl, thiophen-4-yl, or thiazol-2-yl thereof; the variable Het¹ represents pyridine, imidazole, 3,4,5,6-tetrahydro-pyridinyl, indole, 4,5-dihydro-1H-imidazole, benzimidazol, or pyrimidine thereof.

The withdrawn compounds/compositions contain varying heterocycle or heteroaryl of the variable Het or Het¹ of the formula (I), (Ij), (IIa) or X having morpholine, azepane, or piperazine moiety of Groups II-III, which differ from those of the elected invention having indole or pyridine moiety, which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classifications of these functional groups in the U.S. classification system, i.e., class 544 subclass 106(+) (morpholine), class 540 subclass 450(+) (azepane), class 544 subclass (336+) (piperazine), etc. Therefore, again, the compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in common structure and composition and have been restricted properly.

The group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

Claims 1-5, 7-9 and 14-21, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 1-5, 7-9 and 14-21, in part, not embraced in above elected subject matter, and claims 6, 10-13 and 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

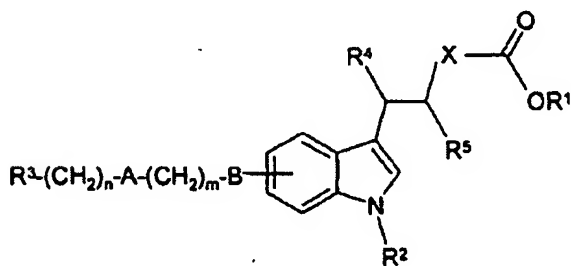
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 7-9 and 14-21 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Brooks et al. US 2004/0063790 A1. Brooks et al. is 102(e) reference.

Applicants claim indole compounds/compositions of formula (I) or (Ij), i.e.,



as integrin inhibitors, see claims 1 and 20.

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Dependent claims 2-5, 7-9 and 14-21 further limit a number of variables, i.e., the variable X is a direct bond.

Brooks et al. disclose two compounds, i.e., 1H-Indole-3-propanoic acid, beta-phenyl-6-[3-(2-pyridinylamino)propoxy]-; and 2,1,3-Benzothiadiazole-5-propanoic acid, beta-[6-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-1H-indol-3-yl]-, see column 51, i.e., claim 5 and 7. Brooks et al. compounds clearly anticipate the instant compounds of formula (I) or (Ij), wherein the variable B is O; the variable m is 3 or 2; the variable A is a bond or NH; the variable n is 0; the variable R³ is Het¹, and Het¹ represents pyridine or pyridine substituted with NHZ, and the variable Z is alkyl (i.e., methyl); the variables R¹, R² and R⁵ independently is H; the variable X is a direct bond; the variable R⁴ represents -(CH₂)_o-Ar, and the variable o is 0, and Ar is phenyl; or the variable R⁴ represents Het, and Het is benzothiadiazole. Dependent claims 2-5, 7-9 and 14-21 are also rejected along with claim 1 under 35 U.S.C. 102(a) or (e).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

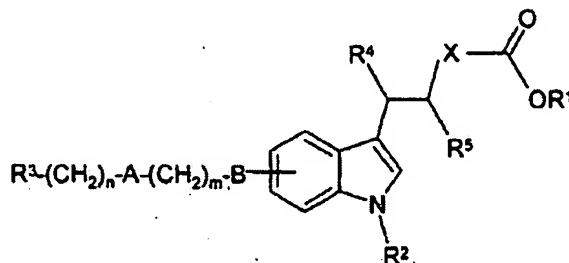
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-5, 7-9 and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al. US 2004/0063790 A1. Brooks et al. is 102(e) reference.

Applicants claim a compound/compositions of formula (I) or (Ij) as integrin



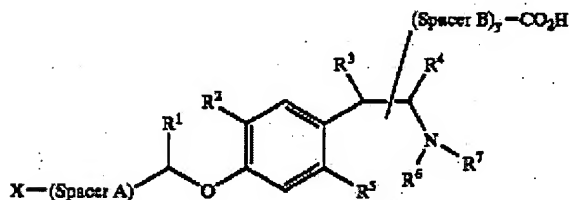
inhibitors, i.e.,

. Dependent claims 2-5, 7-9

and 14-21 further limit a number of variables, i.e., the variable X is a direct bond.

Determination of the scope and content of the prior art (MPEP §2141.01)

Brooks et al. disclose a compound of formula (I), i.e.,



, as integrin inhibitors (i.e., $\alpha v\beta 3$ antagonists),

wherein the variable R^5 and R^6 together form a covalent bond, and the variable R^3 and R^4 together form a covalent bond (i.e., with the fused phenyl forms an indole moiety); the variable Space B is $-\text{CH}(R^8)\text{CH}_2-$, and the variable R^8 is 5-benzo-2,1, 3-thiadiazolyl, and the variable y is 1; the variable R^1 and R^2 independently represents hydrogen; the variable Space A represents $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, or $-\text{CH}_2\text{CH}_2\text{CH}_2-$; the variable X is 2-imidazolyl or 2-pyridyl, see columns 50-51. A number of compounds have been specifically exemplified, see columns 51-52.

Determination of the difference between the prior art and the claims (MPEP**§2141.02)**

The difference between instant claims and Brooks et al. is that the instant variable Het¹ represents pyridine, imidazole, 3,4,5,6-tetrahydro-pyridinyl, indole, 4,5-dihydro-1H-imidazole, benzimidazol, or pyrimidine, while Brooks et al. represents pyridine or imidazole at the same position.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims -5, 7-9 and 14-21 prima facie obvious because one would be motivated to employ the compounds/compositions of Brooks et al. to obtain instant claimed compounds/compositions of formula (I) or (Ij), wherein the variable Het represents benzothiadiazole, 1,3-dioxane, indol-2-yl, pyrrol-2-yl, pyridin-4-yl, thiophen-4-yl, or thiazol-2-yl thereof; the variable Het¹ represents pyridine, imidazole, 3,4,5,6-tetrahydro-pyridinyl, indole, 4,5-dihydro-1H-imidazole, benzimidazol, or pyrimidine thereof. Dependent claims 2-5, 7-9 and 14-21 of claim 1 are also rejected along with claim 1 under 35 U.S.C. 103(a) as the same reasons above.

The motivation to make the claimed products derives from the expectation that the instant claimed compounds/compositions derived from known Brooks et al. compounds would possess similar activities (i.e., integrin inhibitors or $\alpha\beta 3$ antagonists) to that which is claimed in the reference.

Double Patenting

8. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

9. Claims 5 and 17 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 5 of prior Wiesner et al. U.S. Patent No. 6,743,810. This is a double patenting rejection. The instant claimed two compounds, i.e., 3-phenyl-3-{6-[3-(pyridin-2-ylamino)propoxy]-1H-indol-3-yl} propionic acid, and 3-(benzo[1,2,5]thiadiazol-5-yl)-3-{6-[2-(6-methylamino-pyridin-2-yl)-ethyloxy]-indol-3-yl}-propionic acid of claims 5 and 17 have been claimed by Wiesner et al. Elimination of the two compounds in claim 5 and cancellation of claim 17 would obviate the rejection.

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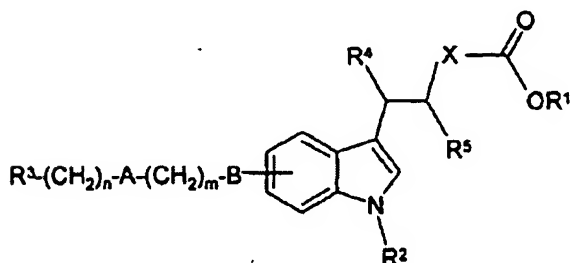
10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-5, 7-9 and 14-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 9 of Wiesner et al. U.S. Patent No. 6,743,810. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

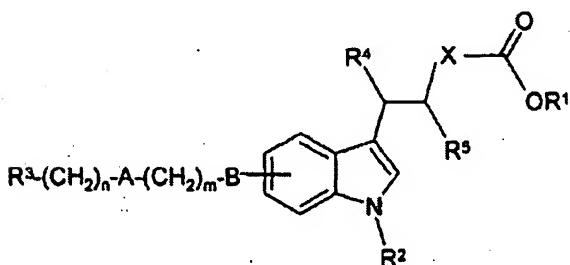
Applicants claim compounds/compositions of formula (I) or (Ij), i.e.,



as agents treating heart diseases, see

claims 1 and 20. The instant compounds have been found on pages 7-86 of the specification. Dependent claims 2-5, 7-9 and 14-21 further limit a number of variables, i.e., the variable X is a direct bond.

Wiesner et al. claim compounds/compositions of formula (I) agents treating heart diseases, i.e.,



, wherein the variable R³ is Het¹, and Het¹

represents pyridine, 3,4,5,6-tetrahydro-pyridinyl, or dihydropyridine; the variable R⁴ or R⁵ independently represents Het, and Het represents benzothiadiazole, 1,3-dioxane, indol-2-yl, pyrrol-2-yl, pyridin-4-yl, or thiazol-2-yl thereof.

The difference between the instant claims and Wiesner et al. is that the instant variable Het¹ represents pyridine, imidazole, 3,4,5,6-tetrahydro-pyridinyl, indole, 4,5-dihydro-1H-imidazole, benzimidazol, or pyrimidine, while Wiesner et al. represents pyridine, dihydropyridine or tetrahydropyridine at the same position.

One having ordinary skill in the art would find the instant claims 1-5, 7-9 and 14-21 prima facie obvious **because** one would be motivated to employ the compounds/compositions of Wiesner et al. to obtain the instant compounds/compositions of formula (I) or (Ij), wherein the variable Het represents benzothiadiazole, 1,3-dioxane, indol-2-yl, pyrrol-2-yl, pyridin-4-yl, thiophen-4-yl, or thiazol-2-yl thereof; the variable Het¹ represents pyridine, imidazole, 3,4,5,6-tetrahydro-pyridinyl, indole, 4,5-dihydro-1H-imidazole, benzimidazol, or pyrimidine thereof. Dependent claims 2-5, 7-9 and 14-21 of claim 1 are also rejected along with claim 1 under the obviousness-type double patenting over Wiesner et al.

The motivation to obtain the claimed compounds/compositions of formula (I) or (Ij) derives from known Wiesner et al. compounds/compositions would possess similar activities (i.e., treating heart diseases) to that which is claimed in the reference.

Claim Objections

12. Claims 1-5, 7-9, 14-21 are objected to as containing non-elected subject matter, i.e., heterocyclic radical, heteroary, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on the pages 2-3 *supra*.

13. Claims 7-9 are objected. Since claims 7-9 are drawn to a pharmaceutical compositions, therefore, amendment of claims 7-9 as pharmaceutical compositions claims would obviate the objection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

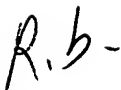
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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A handwritten signature in black ink, appearing to read "Joseph K. McKane", written over a horizontal line.

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626

Handwritten initials "R.b." in black ink.

Robert Shiao, Ph.D.
Patent Examiner
Art Unit 1626

June 15, 2006